...NT COOPERATION TREA...

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 31 July 2000 (31.07.00)	
International application No. PCT/DK99/00589	**Applicant's or agent's file reference** P 1999 01276 WO
International filing date (day/month/year) 29 October 1999 (29.10.99)	**Priority date** (day/month/year) 30 October 1998 (30.10.98)
Applicant RIJKHOFF, Nico, J., M. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

30 May 2000 (30.05.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer C. Cupello
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

HOFMAN-BANG A/S
Hans Bekkevolds Allé 7
DK-2900 Hellerup
DANEMARK

Date of mailing (day/month/year)
31 July 2000 (31.07.00)

Applicant's or agent's file reference
P 1999 01276 WO

IMPORTANT NOTIFICATION

International application No.
PCT/DK99/00589

International filing date (day/month/year)
29 October 1999 (29.10.99)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address

HOFMAN-BANG A/S
Ryesgade 3
P.O. Box 5020
DK-8100 Aarhus C
Denmark

State of Nationality:
State of Residence:
Telephone No.: +45 86 20 22 22
Facsimile No.: +45 86 20 22 10
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address

HOFMAN-BANG A/S
Hans Bekkevolds Allé 7
DK-2900 Hellerup
Denmark

State of Nationality:
State of Residence:
Telephone No.: +45 39 48 8000
Facsimile No.: +45 39 48 8080
Teleprinter No.:

3. Further observations, if necessary:

The new agent's address on the Demand has been considered as a change under Rule 92bis. In case of disagreement, the International Bureau should be notified immediately.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
C. Cupello

Telephone No.: (41-22) 338.83.38

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

HOFMAN-BANG A/S
Hans Bekkevolds Allé 7
DK-2900 Hellerup
DANEMARK

Date of mailing (day/month/year)
29 March 2001 (29.03.01)

Applicant's or agent's file reference
P 1999 01276 WO

IMPORTANT NOTIFICATION

International application No.
PCT/DK99/00589

International filing date (day/month/year)
29 October 1999 (29.10.99)

1. The following indications appeared on record concerning:

[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address
JEZERNICK, Saso
Lenggstrasse 70/605
CH-8008 Zürich
Switzerland

State of Nationality: SI
State of Residence: CH
Telephone No.:
Facsimile No.:
Teleprinter No.:

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [X] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address
JEZERNIK, Saso
Lenggstrasse 70/605
CH-8008 Zürich
Switzerland

State of Nationality:
State of Residence:
Telephone No.:
Facsimile No.:
Teleprinter No.:

3. Further observations, if necessary:
Correction in name.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
J. Leitao

Telephone No.: (41-22) 338.83.38

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For Receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* P 1999 01276 WO

Box No. I TITLE OF INVENTION

A method to control an overactive bladder

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

Aalborg University
Frederik Bajers Vej 7 D-3
DK-9220 Aalborg Ø
DENMARK

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(that is, country)* of nationality: DK Denmark

State *(that is, country)* of residence: DK Denmark

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

RIJKHOFF, Nico J.M.
Færøgade 53 st.th.
DK-9000 Aalborg
DENMARK

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: NL Dutch

State *(that is, country)* of residence: DK Denmark

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Hofman-Bang A/S
Ryesgade 3
P.O. Box 5020
DK-8100 Aarhus C

Telephone No. +45 86 20 22 22

Facsimile No. +45 86 20 22 10

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. II: FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SINKJÆR, Thomas
Nørgaardsvej 3A
DK-9260 Gistrup Denmark
DENMARK

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: DK Denmark

State *(that is, country)* of residence: DK Denmark

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

JEZERNICK, Saso
Lenggstrasse 70/605
CH-8008 Zürich
SWITZERLAND

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: SI Slovenia

State *(that is, country)* of residence: CH Schwitzerland

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

GRILL, Warren
3040 Washington Boulevard
Cleveland Heights OH 44118
USA

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: US USA

State *(that is, country)* of residence: US USA

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of:
- ☐ all designated States
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF STATES

The following designations are made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

- ☒ AP **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ EA **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ EP **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ OA **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- ☒ AE United Arab Emirates
- ☒ AL Albania .....
- ☒ AM Armenia .....
- ☒ AT Austria and utility model
- ☒ AU Australia .....
- ☒ AZ Azerbaijan
- ☒ BA Bosnia and Herzegovina .....
- ☒ BB Barbados
- ☒ BG Bulgaria .....
- ☒ BR Brazil .....
- ☒ BY Belarus .....
- ☒ CA Canada
- ☒ CH and LI Switzerland and Liechtenstein
- ☒ CN China .....
- ☒ CU Cuba .....
- ☒ CZ Czech Republic and utility model
- ☒ DE Germany and utility model
- ☒ DK Denmark and utility model
- ☒ EE Estonia and utility model
- ☒ ES Spain .....
- ☒ FI Finland and utility model
- ☒ GB United Kingdom
- ☒ GD Grenada
- ☒ GE Georgia .....
- ☒ GH Ghana .....
- ☒ GM Gambia
- ☒ HR Croatia .....
- ☒ HU Hungary .....
- ☒ ID Indonesia
- ☒ IL Israel .....
- ☒ IN India .....
- ☒ IS Iceland
- ☒ JP Japan .....
- ☒ KE Kenya .....
- ☒ KG Kyrgyzstan .....
- ☒ KP Democratic People's Republic of Korea .....
- ☒ KR Republic of Korea .....
- ☒ KZ Kazakhstan .....
- ☒ LC Saint Lucia
- ☒ LK Sri Lanka
- ☒ LR Liberia
- ☒ LS Lesotho .....
- ☒ LT Lithuania
- ☒ LU Luxembourg
- ☒ LV Latvia
- ☒ MD Republic of Moldova .....
- ☒ MG Madagascar .....
- ☒ MK The former Yugoslav Republic of Macedonia .....
- ☒ MN Mongolia
- ☒ MW Malawi .....
- ☒ MX Mexico .....
- ☒ NO Norway
- ☒ NZ New Zealand .....
- ☒ PL Poland .....
- ☒ PT Portugal .....
- ☒ RO Romania
- ☒ RU Russian Federation .....
- ☒ SD Sudan
- ☒ SE Sweden
- ☒ SG Singapore
- ☒ SI Slovenia .....
- ☒ SK Slovakia and utility model
- ☒ SL Sierra Leone ...
- ☒ TJ Tajikistan .....
- ☒ TM Turkmenistan .....
- ☒ TR Turkey .....
- ☒ TT Trinidad and Tobago .....
- ☒ UA Ukraine .....
- ☒ UG Uganda .....
- ☒ US United States of America .....
- ☒ UZ Uzbekistan .....
- ☒ VN Viet Nam .....
- ☒ YU Yugoslavia .....
- ☒ ZA South Africa .....
- ☒ ZW Zimbabwe .....

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- ☐ .....
- ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 30 October 1998	PA 1998 01396	DK Denmark		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

** Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):* ISA/ SE

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*
Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	:	4
description (excluding sequence listing part)	:	9
claims	:	4
abstract	:	
drawings	:	3
sequence listing part of description	:	1
Total number of sheets	:	21

This international application is **accompanied by** the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other *(specify)*:

Figure of the drawings which should accompany the abstract: –

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Aarhus C, 29 October 1999

(Henrik Pedersen)
Hofman-Bang A/S

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA/	6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

[redacted]ENT COOPERATION TREA[redacted]

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF RECORD COPY

(PCT Rule 24.2(a))

To:

HOFMAN-BANG A/S
Ryesgade 3
P.O. Box 5020
DK-8100 Aarhus C
DANEMARK

Date of mailing (day/month/year)	IMPORTANT NOTIFICATION
24 November 1999 (24.11.99)	
Applicant's or agent's file reference	**International application No.**
P 1999 01276 WO	PCT/DK99/00589

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

AALBORG UNIVERSITY (for all designated States except US)
RIJKHOFF, Nico, J., M. et al (for US)

International filing date	:	29 October 1999 (29.10.99)
Priority date(s) claimed	:	30 October 1998 (30.10.98)
Date of receipt of the record copy by the International Bureau	:	16 November 1999 (16.11.99)
List of designated Offices	:	

AP :GH,GM,KE,LS,MW,SD,SL,SZ,TZ,UG,ZW
EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
EP :AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
OA :BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG
National :AE,AL,AM,AT,AU,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CU,CZ,DE,DK,EE,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KP,KR,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,US,UZ,VN,YU,ZA,ZW

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

[X] time limits for entry into the national phase

[X] confirmation of precautionary designations

[X] requirements regarding priority documents

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:

J. Leitao

Telephone No. (41-22) 338.83.38

INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is **20 MONTHS** from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, **30 MONTHS** from the priority date, provided that the election is made before the expiration of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. **It is the applicant's responsibility** to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national phase.

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

GR and ES became bound by PCT Chapter II on 7 September 1996 and 6 September 1997, respectively, and may, therefore, be elected in a demand or a later election filed on or after 7 September 1996 and 6 September 1997, respectively, regardless of the filing date of the international application. (See second paragraph above.)

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents, the following is recalled.

Where the priority of an earlier national, regional or international application is claimed, the applicant must submit a copy of the said earlier application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date, provided that any such priority document may still be submitted to the International Bureau before that date of international publication of the international application, in which case that document will be considered to have been received by the International Bureau on the last day of the 16-month time limit (Rule 17.1(a)).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such request must be made before the expiration of the 16-month time limit and may be subjected by the receiving Office to the payment of a fee (Rule 17.1(b)).

If the priority document concerned is not submitted to the International Bureau or if the request to the receiving Office to prepare and transmit the priority document has not been made (and the corresponding fee, if any, paid) within the applicable time limit indicated under the preceding paragraphs, any designated State may disregard the priority claim, provided that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity to furnish the priority document within a time limit which is reasonable under the circumstances.

Where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.

WO 00/25859
PCT/DK99/00589

→ BOK/UC

[redacted]NT COOPERATION TREA[redacted]

BOK

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:
HOFMAN-BANG A/S
Ryesgade 3
P.O. Box 5020
DK-8100 Aarhus C
DANEMARK

Date of mailing (day/month/year) 11 May 2000 (11.05.00)	
Applicant's or agent's file reference P 1999 01276 WO	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/DK99/00589	29 October 1999 (29.10.99)	30 October 1998 (30.10.98)

Applicant
AALBORG UNIVERSITY et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,CN,JP,KP,KR,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CU,CZ,DE,DK,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,
   HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,PL,PT,
   RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   11 May 2000 (11.05.00) under No. WO 00/25859

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

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PATENT COOPERATION TREATY

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

15

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
P 1999 01276 WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DK99/00589	29/10/1999	30/10/1998
International Patent Classification (IPC) or national classification and IPC A61N1/36		
Applicant AALBORG UNIVERSITY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30/05/2000	17.11.2000
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Schoeffmann, H Telephone No. +49 89 2399 2625

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK99/00589

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-10 as originally filed

Claims, No.:

1-21 with telefax of 30/05/2000

Drawings, sheets:

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 6-21.

because:

☒ the said international application, or the said claims Nos. 6-11,15-21 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 12-14 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-5

	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-5
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-5
	No:	Claims	

2. Citations and explanations
see separate sheet

ad III:

1. For the assessment of the present claims 6-11,15-21 on the question whether they are industrially applicable, no unified criteria exist in the PCT. The IPEA therefore is not required to carry out an examination on these claims (Cf. Rule 67.1(iv) PCT).

   The patentability may be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to methods of treatment of the human or animal body by surgery or therapy and diagnostic methods practised on the human or animal body.

   The above claims pertain to a method of estimating bladder volume (claims 6-11) and to a method of controlling an overactive bladder (claims 15-21). Both methods require the implantation of electrodes in order to detect nerve signals from nerves innervating the bladder. The method step of detecting nerve signals from nerves innervating the bladder thus, implicitly, requires a surgical step. By presence of a surgical step, regardless whether explicit or implicit, the methods as a whole are rendered surgical. Methods of surgery however may not be regarded as an invention susceptible of industrial application.

   Moreover, method claims 15-21 define a method of treatment by neurostimulation which is practised on the living human or animal body which, therefore, also cannot be regarded as an invention susceptible of industrial application.

2. Claim 12 is drafted by definition of the result to be achieved without specifying the necessary means in clear technical terms so that an objection under Art.6 PCT for lack of clarity is raisable. The passages concerned are:

   - a unit capable of detecting a bladder event from the nerve signals (how? and which bladder event?), the unit being capable of generating a stimulation signal (which one and applied to where?) in response thereto (how?)

   Claims 13 and 14 do not illustrate the above indicated obscurity, therefore, when combined with the subject-matter of claim 12 still fails to define clear subject-matter.

Claim 12 and claims 13,14 dependent thereon thus do not meet the requirement of Art.6 PCT so that no statement with respect to the requirements of Art.33 PCT can be given.

ad V:

1. Reference is made to the following documents:

   D1: 'Mechanosensitive Properties of Pelvic Nerve Afferent Fibers Innervating the Urinary Bladder of the Rat','J.N. SENGUPTA ET AL.','JOURNAL OF NEUROPHYSIOLOGY,',",72/5/00-11-1994,2420-2430,

2. From document D1, which is considered as the closest prior art, the correlation between bladder distension or contraction and activities of the pelvic nerve afferent fibers is known (cf. sentence linking the two columns on page 2426 of D1). As apparent from fig.7A,B intravesical pressure is proportional to both the amplitude of the nerve signal (fig.7A) and frequency of nerve activity (fig.7B). A rough correlation between intravesical pressure and human bladder volume is also apparent (cf. page 2426, 2nd paragraph from page bottom: eg. 250-300 ml correspond to intravesical pressure of 5-15 mmHg).

   Since however the purpose of the D1 document was to investigate the responses of the pelvic nerve afferent fibers to artificially induced urinary bladder distension and contraction (cf. page 2421, left col., 1st paragraph), a device, according to claim 1, for estimating bladder volume by detecting nerve signals cannot be derived therefrom without hindsight. Therefore claim 1 is considered to meet the requirements of Art.33(2)-(4) PCT, as are claims 2-5 dependent thereon.

~~Claims:~~ What is claimed is:

1. An apparatus for estimating bladder volume, comprising:

- sensor means for sensing nerve signals from nerves innervating the bladder;

- a unit capable of estimating bladder volume in response to the detected signals using signal-processing methods.

2. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from the amplitude of the detected nerve signal.

3. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from the time between two detected nerve signals derived from two consecutive detrusor contractions.

4. An apparatus as defined in claim 1, wherein the unit is capable of deriving a bladder volume from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.

5. An apparatus as defined in any of claims 1 to 4, further comprising transmitting means, receiving means and actuating means,

- said transmitting means together with the unit being capable of being placed inside the body of a user;

- said receiving means, when placed outside the body of a user, being capable of receiving a signal from said transmitting means, when placed inside the body of a user, and passing the signal to actuating means for alerting the user that a given threshold value for the bladder volume has been reached.

6. A non-therapeutic method to estimate bladder volume, comprising the steps:

- detecting nerve signals from nerves innervating the bladder;

- estimate bladder volume in response to the detected signals using signal-processing methods.

7. A method as defined in claim 6, wherein the bladder volume is estimated from the amplitude of the detected nerve signal.

8. A method as defined in claim 6, wherein the bladder volume is estimated from the time between two detected nerve signals derived from two consecutive detrusor contractions.

9. A method as defined in claim 6, wherein the bladder volume is estimated from both the amplitude of the detected nerve signal and from the time between two detected nerve signals derived from two consecutive detrusor contractions.

10. A method as defined in any of claims 6 to 9,

comprising the further steps of: transmitting, from a transmitter placed inside the body of a user, a signal when a predetermined threshold is exceeded, receiving the signal with a receiver placed outside the body of a user, actuating an alert in response to the received signal for alerting the user that a given threshold value for the bladder volume has been reached.

11. A method to estimate bladder volume, comprising the steps:

- detecting nerve signals from nerves innervating the bladder;

- estimate bladder volume in response to the detected signals using signal-processing methods.

12. An apparatus for controlling an overactive bladder, comprising:

- sensor means for sensing nerve signals from nerves innervating the bladder;

- a unit capable of detecting a bladder event from the nerve signals, the unit being capable of generating a stimulating signal in response thereto; and

- means for stimulation of nerves using the generated stimulating signal in order to inhibit detrusor contraction.

13. An apparatus as defined in claim 12, comprising

a single nerve electrode serving as both a sensor means and stimulation means, said nerve electrode being adapted to be implanted on either the intradural dorsal sacral nerve roots (S2-S4) or the extradural sacral nerve root (S2-S4).

14. An apparatus as defined in claim 12 or 13, wherein said sensor means is capable of sensing two different nerve signals, and where the unit is capable of detecting a bladder event from said two different nerve signals.

15. A method to control an overactive bladder, comprising the steps:

- detecting nerve signals from nerves innervating the bladder;

- detecting a bladder event from the nerve signals;

- generating electrical pulses in response to the detected event;

- stimulating afferent nerves using the generated electrical pulses in order to inhibit detrusor contraction of the bladder.

16. A method as defined in claim 15, wherein the detected nerve signals primarily come from afferents innervating mechanoreceptors in the bladder wall.

17. A method as defined in claim 15, wherein the de-

tected nerve signals come from efferent nerve fibres innervating the bladder.

18. A method as defined in claim 15, wherein two different signals are used to detect a detrusor contraction, the first signals coming from afferent nerves innervating the bladder, and the second signals coming from efferent nerves innervating the detrusor muscle.

19. A method as defined in any of claims 15 to 18, wherein neural circuits inhibiting bladder contraction are stimulated by activating an inhibitory spinal reflex by stimulating afferent nerve fibres innervating mechanoreceptors located in the glans of the penis or clitoris.

20. A method as defined in claim 19, wherein a stimulation electrode is located at a dorsal penile/clitoris nerve, a pudendal nerve, a extradural sacral nerve root or an intradural dorsal sacral nerve root.

21. A method as defined in claim 15, wherein both a detecting electrode and a stimulation electrode is located at either the intradural dorsal sacral nerve roots (S2-S4) or the extradural sacral nerve root (S2-S4).

Add A1

add B15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00589

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61N 1/36
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4607639 A (E.A. TANAGHO ET AL.), 26 August 1986 (26.08.86), column 2, line 3 - line 11; column 7, line 59 - line 64	1-16
D,Y	Journal of Neurophysiology, Volume 72, No 5, November 1994, J.N. Sengupta et al., "Mechanosensitive Properties of Pelvic Nerve Afferent Fibers Innervating the Urinary Bladder of the Rat" page 2420 - page 2430	1-16
A	WO 9516491 A1 (THOMAS JEFFERSON UNIVERSITY), 22 June 1995 (22.06.95), abstract, table	1-16

[ ] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" erlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 January 2000	16 -02- 2000
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Nikolaj Hautaviita/AE Telephone No. +46 8 782 25 00

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK99/00589

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-16
because they relate to subject matter not required to be searched by this Authority, namely:

See next sheet.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK99/00589

Claims 1-16 relates to a method of treatment of the human or animal body by surgery or by therapy diagnostic methods practiced on the human or animal body/ Rule. 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the device described in the method.

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.
PCT/DK 99/00589

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4607639 A	26/08/86	US 4703755 A	03/11/87
		US 4739764 A	26/04/88
		US 4771779 A	20/09/88
		AT 55697 T	15/09/90
		EP 0245547 A,B	19/11/87
		SE 0245547 T3	
WO 9516491 A1	22/06/95	AU 680993 B	14/08/97
		AU 1431295 A	03/07/95
		CA 2178904 A	22/06/95
		EP 0744980 A	04/12/96
		JP 2810793 B	15/10/98
		JP 9507401 T	29/07/97
		US 5370670 A	06/12/94
		US 5752978 A	19/05/98

PCT

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : A61N 1/36

A1

(11) International Publication Number: WO 00/25859

(43) International Publication Date: 11 May 2000 (11.05.00)

(21) International Application Number: PCT/DK99/00589

(22) International Filing Date: 29 October 1999 (29.10.99)

(30) Priority Data:
PA 1998 01396 30 October 1998 (30.10.98) DK

(71) Applicant *(for all designated States except US)*: AALBORG UNIVERSITY [DK/DK]; Frederik Bajers Vej 7 D-3, DK-9220 Aalborg Ø (DK).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: RIJKHOFF, Nico, J., M. [NL/DK]; Færøgade 53 st.th., DK-9000 Aalborg (DK). SINKJÆR, Thomas [DK/DK]; Nørgaardsvej 3A, DK-9260 Gistrup (DK). JEZERNICK, Saso [SI/CH]; Lenggstrasse 70/605, CH-8008 Zürich (CH). GRILL, Warren [US/US]; 3040 Washington Boulevard, Cleveland Heights, OH 44118 (US).

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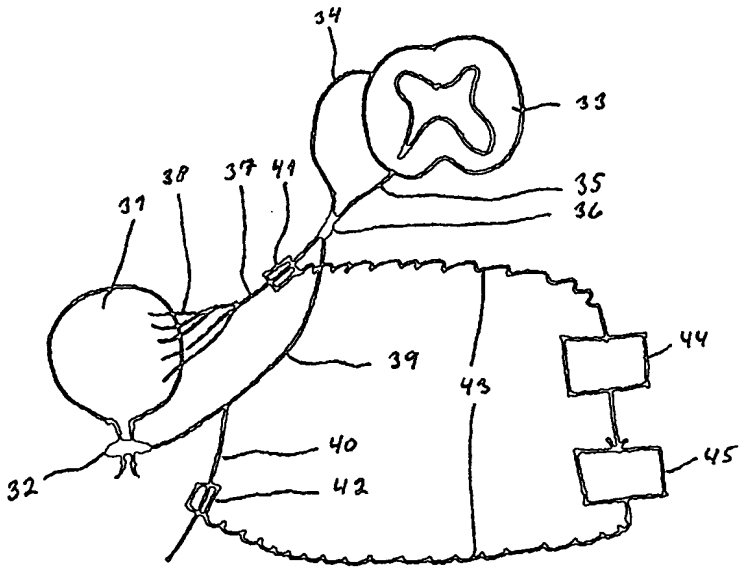
(81) Designated States: AE, AL, AM, AT, AT (Utility model), AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ (Utility model), DE, DE (Utility model), DK, DK (Utility model), EE, EE (Utility model), ES, FI, FI (Utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK (Utility model), SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: A METHOD TO CONTROL AN OVERACTIVE BLADDER



(57) Abstract

This application concerns a method to control an overactive bladder and to estimate bladder volume, comprising an implanted sensor, which sensor comprises at least one nerve electrode to sense electrical signals, means for stimulation of nerves to inhibit detrusor contraction, an electronic unit to detect events from nerve signals and generate electrical pulses for stimulating nerves. The object of the invention is treatment of involuntary loss of urine (incontinence) due to involuntary detrusor contractions (detrusor overactivity). Another object of the invention is estimation of bladder volume. This finds particular application in patients who use aids to empty their bladder e.g. intermittent catherisation or electrical stimulation.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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A method to control an overactive bladder.

This application concerns a method to control an overactive bladder and to estimate bladder volume, comprising an implanted sensor, which sensor comprises at least one nerve electrode to sense electrical signals, means for stimulation of nerves to inhibit detrusor contraction, an electronic unit to detect events from nerve signals and generate electrical pulses for stimulating nerves.

US 4,406,228 discloses a system that purportedly conditions pelvic floor musculature by means of neurostimulation for the purpose of controlling urinary loss. Such system includes stimulation apparatus for applying electrical pulses to electrodes implanted in the abdominal region or to a plug positioned in an anus. The plug contacts the spincter muscle of the anus for the alleged purpose of inhibiting bladder contraction in response to excitation of the plug.

In this way the bladder volume is not measured, which can lead to bladder over distensions, and can lead to bladder rupture.

The storage phase of the micturition cycle requires a stable bladder with high compliance (i.e. a relaxed bladder) and closed urethral outlet. However, due to the feedback system the bladder may easily become unstable. Any stimulus that elicits a small burst of impulses in the mechanoreceptor afferents, such as coughing and jumping may trigger an involuntary micturition reflex and cause urine leakage. To prevent this from happening the neural control system is equipped with several inhibitory circuits, both at spinal and supraspinal levels, which prevent the detrusor muscle to contract. However, these inhibitory circuits are susceptible to a variety of neu-

rologic disorders. Therefore patients with neurologic disorders frequently suffer from urinary incontinence due to involuntary detrusor contractions.

The impaired storage function could in principle be improved by methods that decrease the sensitivity of the bladder afferents, decrease the activity of the bladder efferents or increase the bladder volume/capacity. Available treatment options are therefore: surgical augmentation of the bladder [Sidi et al., 1990], surgical deafferentation of the bladder [Koldewijn et al., 1994], the use of anticholinergic drugs and the use of intravesical capsaicin [Wiart et al., 1998].

Bladder inhibition by electrical stimulation has been described before [e.g. Vodušek et al., 1988; Wheeler et al., 1992] but only continues stimulation was used, e.i. stimulation is permanent except during voiding.

Reff

Add: T. Lefurge, E. Goodall, K. Horch, L. Stensaas, and A. Schoenberg, "Chronically implanted intrafascicular recording electrodes," *Annals of Biomed. Eng.*, vol. 19, pp. 197-207, 1991.

Add: J.N. Sengupta, G.F. Gebhart, "Mechanosensitive properties of the pelvic nerve afferent fibres innervating the urinary bladder of the rat," J. Neurophysiol., vol. 72, pp. 2420-2430, 1994.

The object of the inventions is:

1) treatment of involuntary loss of urine (incontinence) due to involuntary detrusor contractions (detrusor overactivity)

2) estimation of bladder volume. This finds particular application in patients who use aids to empty their bladder e.g. intermittent catherisation or electrical stimulation.

The invention finds particular application in patients where the involuntary detrusor contraction is associated with a neurologic disorder.

Treatment of detrusor overactivity and extimation of bladder volume can be achieved by a method as described in the first paragraph using a closed loop stimulation system to allow event driven inhibition of the bladder where stimulation is only applied when an undesired bladder contraction occurs, and an implanted sensor comprising at least one nerve electrode to sense electrical signals from nerves innervating the bladder. Sensing electrical signals related to mechanical bladder activity via said sensor, and detecting the onset of a bladder contraction and estimation of bladder volume using signal processing methods, and activating an inhibitory neural circuit by stimulating afferent nerve fibbers, in response to detection of the onset of a bladder contraction.

By this method no nerves has to be cut, and no irreversible surgery has to be done. Stimulation of neural tissue only takes place when needed, and the volume of the bladder is monitored. The present invention uses electrical stimulation to inhibit the bladder. Inhibition of the bladder by electrical stimulation is possible since, besides the mentioned neural inhibitory circuits, additional spinal inhibitory circuits exist to prevent involuntary leakage during e.g. defecation, coitus and physical activity. Activation of the afferent path of these neural circuits has two effects: they activate the in-

hibitory sympathetic neurones to the bladder and they provide central inhibition of the preganglionic detrusor-motoneurons through a direct route in the spinal cord. These additional inhibitory reflexes are not suppressed during micturition, which means that they are quite capable of interrupting a detrusor contraction. Activation of these reflexes by electrical stimulation is a non-destructive alternative method for patients who are refractory to drugs, cannot tolerate the side effects or for other reasons do not accept a drug treatment.

Primalarythe recorded nerve signals comes from afferents innervating mechanoreceptors located in the bladder wall. By detecting the onset of the bladder contraction the stimulator could be activated only when contraction occurs, and continuos stimulation is not necessary. This minimises the risk of neural damages due to the stimulation. In addition, if the patient can sense the stimulation, the duration of stimulation should be minimised to minimise the discomfort.

The step of implanting a sensor might comprise the step of implanting a nerve cuff electrode. The cuff electrode has been used successfully in other applications and has been shown to be safe for human implants.

The step of implanting a sensor might comprise the step of implanting an intrafasicular electrode [Lefurge et al., 1991]. The intrafasicular electrode is flexible and smaller, and might be preferred in locations where limited space is available.

The electrodes can be used to detect efferent or afferent nerve activity. The same electrode could be used to record both types of nerve signals.

The electrode can be placed on a nerve that contains afferent nerve fibres innervating mechanoreceptors located in the bladder. In this way information about the status of the bladder can be obtained .

The electrode can be located at the intradural or extradural dorsal sacral nerve roots. In this way the electrodes can be placed at a mechanical stable position, and the nerve roots are relatively long, which enables easy placement of electrodes.

The electrode can be placed on a nerve that contains efferent nerve fibres innervating the bladder, so bladder activation can be monitored.

The electrode can be located at the intradural or extradural ventral sacral nerve roots. In this way the electrodes can be placed at a mechanical stable position, and the nerve roots are relatively long, which enables easy placement of electrodes.

The electrode might be located at at least one of the preganglionic pelvic nerve branches and postganglionic nerve branches. In this way nerve signals from the bladder can be recorded more selectively without contamination with signals from other organs.

Preferably two different nerve signals can be used to detect a detrusor contraction, where the first signal comes from afferent nerves innervating the bladder, and the second signals comes from efferent nerves innervating the detrusor muscle. In this way the detrusor contraction can be detected more reliable.

Activating a neural circuit that inhibits the bladder contraction can be done by stimulating afferent nerve fibres, innervating mechanoreceptors, located in the glans of the penis or clitoris. In this way an ongoing detrusor contraction can be aborted or stopped and leakage of urine will be prevented.

The bladder volume can be derived from the amplitude of the recorded afferent signal. By measuring of the bladder volume the patient can be informed about his/her bladder volume.

The bladder volume can be derived from the time between 2 consecutive detrusor contractions. By measuring of the bladder volume the patient can be informed about his/her bladder volume.

The bladder volume can be derived form both the amplitude of the recorded nerve signal and the time between 2 consecutive detrusor contractions. This way the bladder volume can be estimated in a more reliable way.

In the following the invention will be detailed described partly with reference to drawings.

Fig.1 shows a block diagram of event driven stimulation system to treat an overactive bladder.

Fig. 2 shows a block diagram of a bladder volume monitoring system.

Fig. 3 shows schematically how the invention is applied.

Mechanoreceptors located in the bladder wall act as tension receptors and respond in graded fashion to increases in bladder volume and intravesical pressure [Sengupta and

Gebhart, 1994]. It has been shown that a close relationship between afferent nerve activity and the pattern of intravesical pressure changes is best observed when the activity of many afferent nerve fibres is summed. Sensor 14 comprises an implantable nerve cuff electrode. This type of electrode surrounds the selected nerve in close proximity so currents generated by the nerve fibres result in sufficient large voltage differences in the volume within the cuff so that they can be detected by the electrode. However, other electrode configurations such as intrafasicular electrodes could also be used to detect the efferent nerve activity. The electrode needs to be placed on a peripheral nerve 15 that contains afferent nerve fibres innervating mechanoreceptors located in the bladder. Possible locations for the electrode are therefore: intradural dorsal sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches. An alternative method to detect a bladder contraction is to record from the efferent nerve fibres that innervate the detrusor muscle. An increase in the efferent signal results in a detrusor contraction so an increased efferent signal indicates a detrusor contraction. Possible locations for the electrode to record efferent signals from peripheral nerve 15 are: intradural ventral sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches.

The output of the sensor 14 is passed through a circuit 13 that includes an amplifier and a filter. The output of circuit 13 is passed to circuit 10, which contains a detection algorithm that allows the detection of the onset of a sudden rise in intravesical pressure or a detrusor contraction. The detection algorithm takes place in a signal processor 10, which will pass a trigger signal to

stimulator 11 when it detects such a pressure rise. The stimulator 11 includes one or more electrodes placed on peripheral sensory nerves 12. The stimulator 11 produces, in response to the trigger signal from circuit 10, an electrical potential difference, which will result in an electrical current through the electrode and adjacent nervous tissue. A rapid change in this electrical current activates or stimulates nerve fibres causing the production of action potentials in peripheral nerve 12. It has been shown that activation of afferent nerve fibres, innervating mechanoreceptors located in the glans of the penis or clitoris, has a strong inhibitory effect on the bladder. To obtain the desired effect of bladder inhibition upon stimulation the afferents should be stimulated somewhere along their course from mechanoreceptors to the sacral spinal cord. This means that possible locations for the electrode to be placed on peripheral nerve 12 are: dorsal penile/clitoris nerve, pudendal nerve, extradural sacral nerve roots (S2-S4) and intradural dorsal sacral nerve roots (S2-S4).

A system for monitoring the bladder volume is shown in FIG.2. Mechanoreceptors located in the bladder wall act as tension receptors and respond in graded fashion to increases in bladder volume and intravesical pressure. It has been shown that a close relationship exist between afferent nerve activity and bladder volume. In addition, bladder volume could be estimated from the time between two consecutive hyperreflexic bladder contractions since the number of contractions per time unit is proportional to the bladder volume. The preferred nerve electrode 25 for this purpose is an implantable nerve cuff electrode, although other electrode configurations could also be used. The sensor 25 comprises an electrode, which needs to be placed on a peripheral sensory nerve 26 that contains afferent nerve fibres innervating mechanoreceptors

located in the bladder. Possible locations for the sensor 25 are therefore: intradural dorsal sacral nerve roots (S2-S4), extradural sacral nerve roots (S2-S4), preganglionic pelvic nerve branches and postganglionic nerve branches. Sensor 25 could be the same one as sensor 14 so the systems of FIG.1 and FIG.2 share the same electrode.

The output of the sensor 25 is passed through a circuit 24 that includes an amplifier and a filter. The output of circuit 24 is passed to signal processing unit 20, which contains an estimation algorithm that allows estimation of bladder volume. If the estimated volume exceeds the volume threshold then a trigger signal will be passed to transmitter 21. Upon receiving a trigger, transmitter 21 sends a signal to receiver 22 using radio waves. Receiver 22 is placed outside the body and will, upon receiving a signal from transmitter 21, pass a signal to actuator 23. Actuator 23 will alert the user that the bladder volume exceeded the volume threshold. Various devices could be used as actuator such as a buzzer, a vibrator, etc.

Fig. 3 shows in detail the elements of the invention. A Bladder 31 with a closing mechanism comprising a sphincter 32 together with the innervating peripheral nerves, which comprises 34 intradural dorsal sacral root 34, intradural ventral sacral root 35, extradural sacral root 36, Preganglionic Pelvic nerve 37, Postganglionic pelvic nerve 38 and Pudendal nerve 39. In addition the dorsal penile/clitoral nerve 40 is shown. These nerves relay information to and from the spinal cord 33. A recording electrode 41 senses information from the nerves 37, and electrical information is transmitted through an electrode lead 43 to a signal processing unit 44, which is connected to a stimulator 45. Signal from stimulator 45 is transmitted through an electrode lead 43 to a stimulation electrode 42, which stimulates nerve 40.

10 Signal processor
11 Stimulator
12 Peripheral sensory nerve
13 Amplifier
14 Sensor
15 Peripheral nerve

20 Signal processor
21 Transmitter
22 Receiver
23 Actuator
24 Amplifier
25 Sensor
26 Peripheral sensory nerve

31 Bladder
32 Sphincter
33 Spinal cord
34 intradural dorsal sacral root
35 intradural ventral sacral root
36 extradural sacral root
37 Preganglionic Pelvic nerve
38 Postganglionic pelvic nerve
39 Pudendal nerve
40 Dorsal penile/clitoral nerve
41 Recording electrode
42 Stimulation Electrode
43 Electrode lead
44 Signal processing unit
45 Stimulator

Claims

1. A method to control an overactive bladder and to estimate bladder volume, comprises: an implanted sensor, which sensor comprises at least one nerve electrode to sense electrical signals,

means for stimulation of nerves to inhibit detrusor contraction,

an electronic unit to detect events from nerve signals and generate electrical pulses for stimulating nerves,

characterized in,

that stimulation is only applied when a bladder contraction occurs,

that the implanted sensor comprising at least one nerve electrode to sense electrical signals from nerves innervating the bladder,

said method comprises the step of:

a) sensing electrical signals related to mechanical bladder activity via said sensor,

b) detecting the onset of a bladder contraction and estimation of bladder volume using signal processing methods,

c) activating an inhibitory spinal reflex by stimulating afferent nerve fibres, in response to detection of the onset of a bladder contraction,

using a closed loop stimulation system to allow event driven inhibition of the bladder.

2. A method of claim 1, **characterized in**, that detected nerve signals primarily comes from afferents innervating mechanoreceptors located in the bladder wall,

3. A method of claim 1 or 2, **characterized in** that the step of implanting a sensor comprises the step of implanting a nerve cuff electrode.

4. A method of one of the claims 1-3, **characterized in**, that the step of implanting a sensor comprises the step of implanting a intrafasicular electrode.

5. A method of one of the claims 1-4, **characterized in**, that the electrodes is used to detect efferent or afferent nerve activity.

6. A method of one of the claims 1-5, **characterized in**, that the electrode is placed on a nerve that contains afferent nerve fibres innervating mechanoreceptors located in the bladder.

7. A method of one of the claims 1-6, **characterized in**, that the electrode is located at the intradural or extradural dorsal sacral nerve roots.

8. A method of one of the claims 1-5, **characterized in**, that the electrode is placed on a nerve that contains efferent nerve fibres innervating the bladder.

9. A method of one of the claims 1-5 and 8, **characterized in**, that the electrode is located at the intradural or extradural ventral sacral nerve roots.

10. A method of one of the claims 1-5 and 6 and 8, **characterized in**, that the electrode is located at least one of the preganglionic pelvic nerve branches or postganglionic nerve branches.

11. A method of one of the claims 1-10, **characterized in**, that 2 different nerve signals is used to detect a detrusor contraction, where the first signal comes from afferent nerves innervating the bladder, and the second signals comes from efferent nerves innervating the detrusor muscle.

12. A method of one of the claims 1-11, **characterized in**, activating neural circuits that inhibit bladder contraction by activating an inhibitory spinal reflex by stimulating afferent nerve fibres, innervating mechanoreceptors located in the glans of the penis or clitoris.

13. A method of claim 12, **characterized in**, that the stimulation electrode is located at a dorsal penile/clitoris nerve, or a pudendal nerve, or a extradural sacral nerve root or a intradural dorsal sacral nerve root.

14. A method of one of the claims 1-13, characterized in, that the bladder volume is derived from the amplitude of the recorded nerve signal.

15. A method of one of the claims 1-14, characterized in, that the bladder volume is derived from the time between 2 consecutive detrusor contractions.

16. A method of claim 14 or 15, characterized in, that the bladder volume is derived form both the amplitude of

the recorded nerve signal and the time between 2 consecutive detrusor contractions.

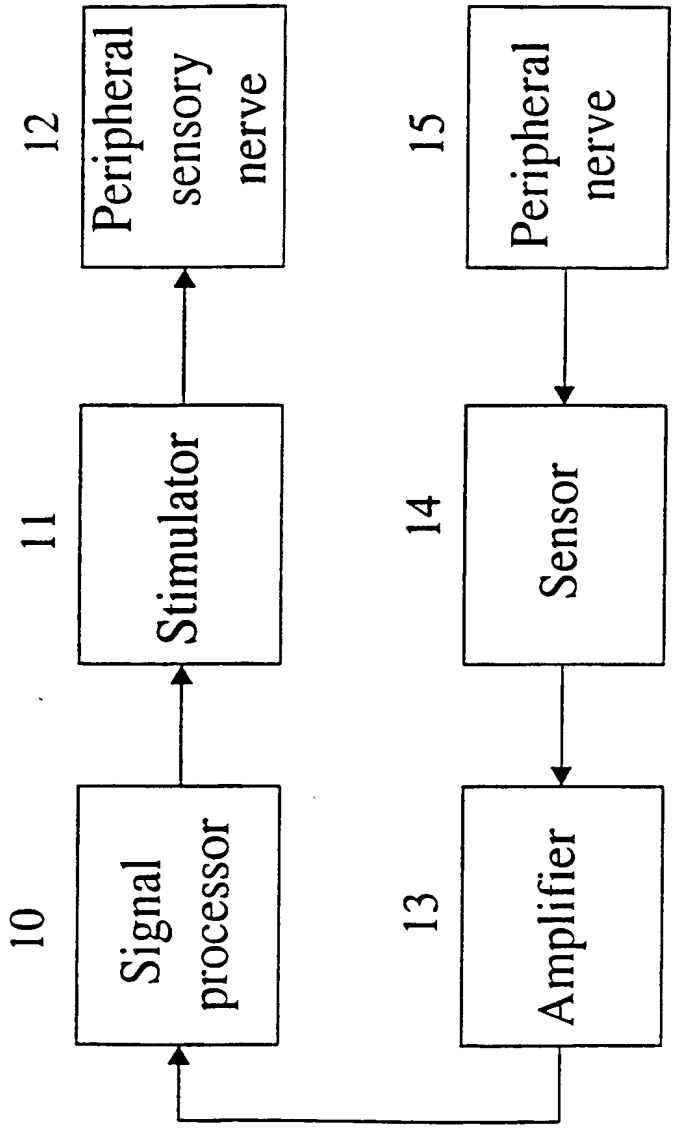

Fig. 1
Bladder patent

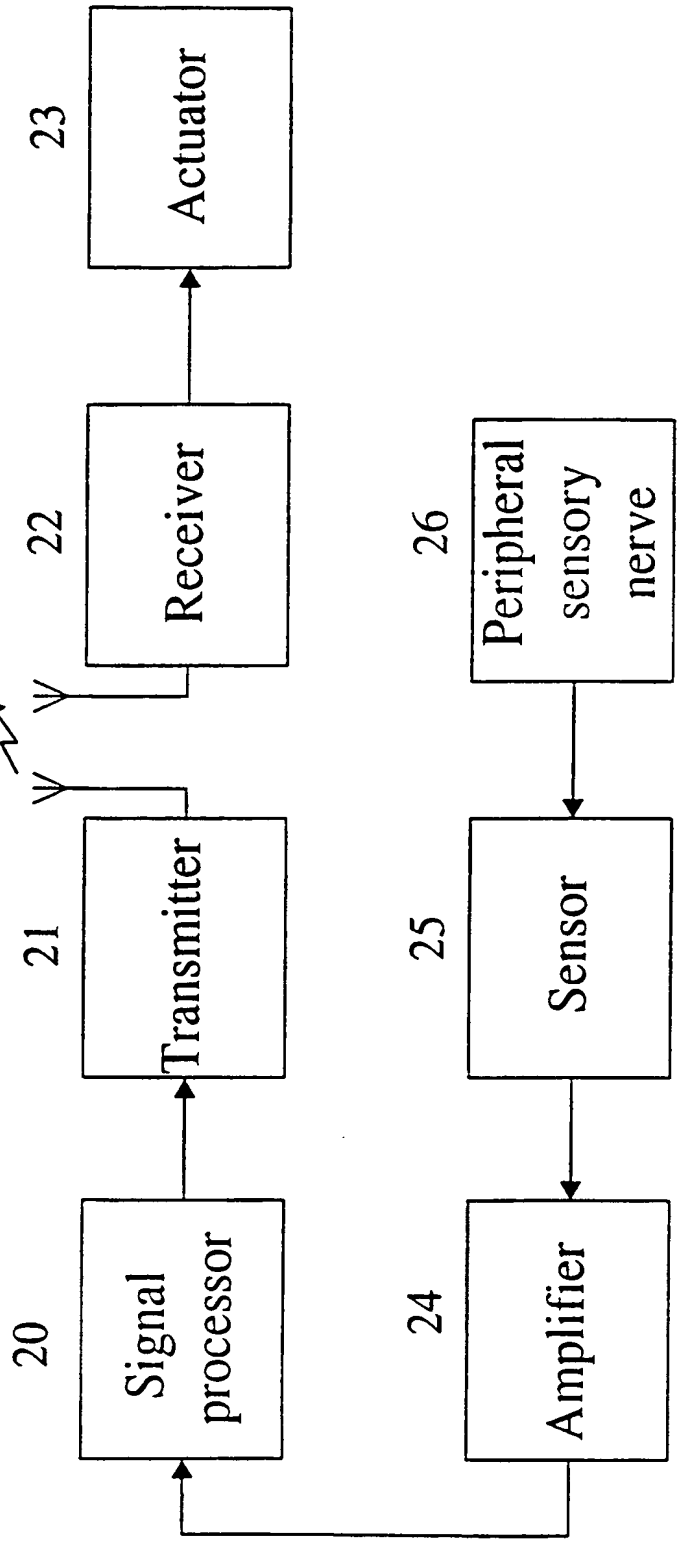

Fig. 2
Bladder patent

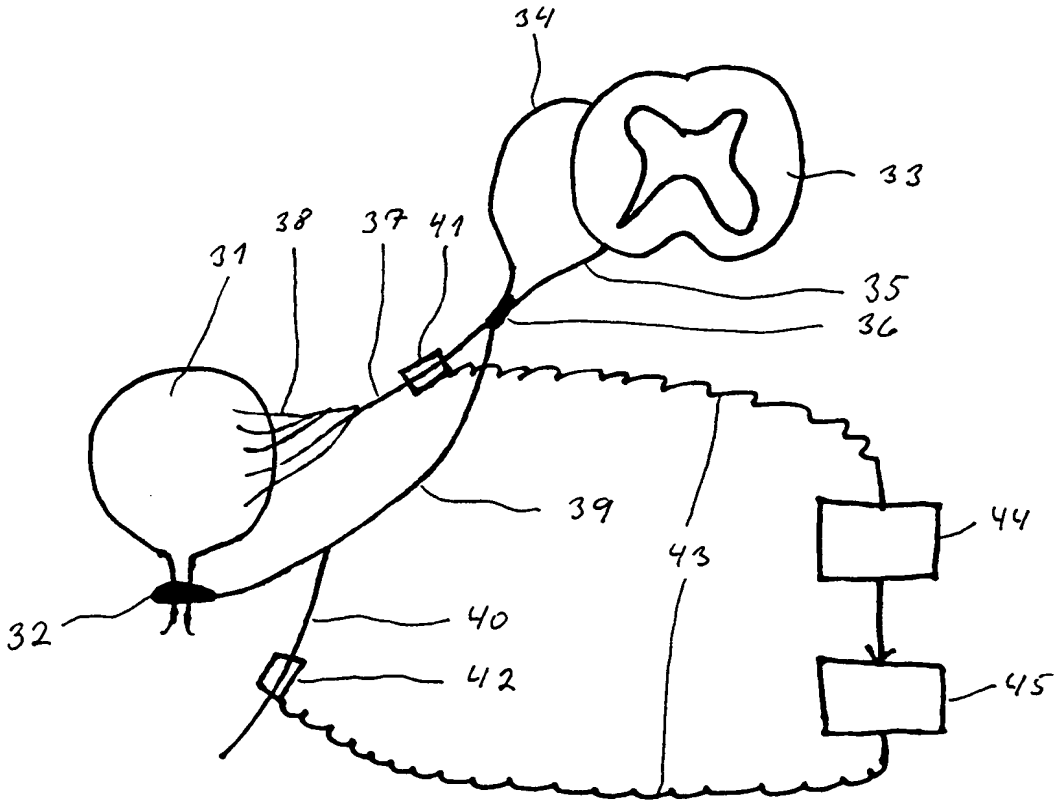

Fig. 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK 99/00589

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61N 1/36
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4607639 A (E.A. TANAGHO ET AL.), 26 August 1986 (26.08.86), column 2, line 3 - line 11; column 7, line 59 - line 64	1-16
D,Y	Journal of Neurophysiology, Volume 72, No 5, November 1994, J.N. Sengupta et al., "Mechanosensitive Properties of Pelvic Nerve Afferent Fibers Innervating the Urinary Bladder of the Rat" page 2420 - page 2430	1-16
A	WO 9516491 A1 (THOMAS JEFFERSON UNIVERSITY), 22 June 1995 (22.06.95), abstract, table	1-16

[ ] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" crlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 January 2000	16 -02- 2000
Name and mailing address of the ISA/ Swedish Patent Office Box 5055, S-102 42 STOCKHOLM Facsimile No. +46 8 666 02 86	Authorized officer Nikolaj Hautaviita/AE Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK99/00589

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-16
because they relate to subject matter not required to be searched by this Authority, namely:

See next sheet.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK99/00589

Claims 1-16 relates to a method of treatment of the human or animal body by surgery or by therapy diagnostic methods practiced on the human or animal body/ Rule. 39.1.(iv). Nevertheless, a search has been executed for these claims. The search has been based on the device described in the method.

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.
PCT/DK 99/00589

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4607639 A	26/08/86	US 4703755 A	03/11/87
		US 4739764 A	26/04/88
		US 4771779 A	20/09/88
		AT 55697 T	15/09/90
		EP 0245547 A,B	19/11/87
		SE 0245547 T3	
WO 9516491 A1	22/06/95	AU 680993 B	14/08/97
		AU 1431295 A	03/07/95
		CA 2178904 A	22/06/95
		EP 0744980 A	04/12/96
		JP 2810793 B	15/10/98
		JP 9507401 T	29/07/97
		US 5370670 A	06/12/94
		US 5752978 A	19/05/98